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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,667	09/18/2003	Wei Gu	MPI99-037P1RCP1CN1M	5794

30405 7590 03/07/2006

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EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/664,667	GU, WEI	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-39 and 41-45* is/are pending in the application.

4a) Of the above claim(s) *42,43 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-39,41 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' amendment filed on 12/16/2005 has been entered. Claims 23-25 and 35-39 have been amended. Claim 40 has been canceled. Claims 41-45 have been added. Claims 23-39 and 41-45 are pending. Claims 23-39, 41, and 44 are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Withdrawn Objections and/or Rejections

The objections to the specification have been withdrawn in view of the amendment to the specification.

The rejection of claims 38-40 under 35 U.S.C. 112, first paragraph, for written description, as set forth in the previous office action, has been withdrawn in view of canceled claim 40 and amended claims 38 and 39.

The rejection of claim 38-40 under 35 U.S.C. 112, second paragraph has been withdrawn in view of canceled claim 40 and amended claims 38 and 39.

The rejection of claims 38-40 under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (EMBL Database, Accession No. AA292507, May 16, 1997) has been withdrawn in view of canceled claim 40 and amended claims 38 and 39.

The objection to claims 23-40 has been withdrawn in view of canceled claim 40 and amended claims.

Claim Rejections under 35 USC § 101

The rejection of claims 23-39 under 35 U.S.C. § 101 is maintained. Claims 41 and 44 are also rejected under 35 U.S.C. § 101 on the same basis. The basis for this rejection is set forth in the previous Office Action (Paper No. 06032005, mailed on 06/13/2005).

Beginning at the 2nd paragraph of page 24 of Applicants' response filed on 12/16/2005, Applicants argue that LGR6 is identified as a particular type of GPCR, having an N-terminal extracellular domain comprising leucine rich repeats, in addition to the standard seven transmembrane portion typical of GPCRs. Applicants submit that LGR6 is a member of GPCR subfamily I, which includes the beta2adrenergic receptor. Applicants further argue that LGR6 was further identified in a subgroup which includes glycoprotein hormone receptors, which activates the Gs-cAMP signal transduction pathway.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. First, as noted in the previous office action, the state of the art is

such that the biological functions of proteins are unpredictable solely based upon sequence homology (Peer Bork and Eugene V. Koonin, Predicting functions from protein sequences--where are the bottlenecks? *Nature Genetics* 18:313-318,1998). The prior art also teaches that sequence-based methods for function prediction are inadequate (*Trends in Biotech* 18: 34-39, 2000) and a change of two-amino acid residues in a protein results, in certain case, in switching the binding of the protein from one receptor to another (Yan et al., *Science* 290: 523-527, 2000). There are putative seven transmembrane molecules, which do not appear to be coupled to a G protein (Ji et al., *J. Biol. Chem.* 273:17299-17302, 1998; in particular, the 3rd paragraph of left column of page 17299).

Secondly, even if the sequence homology can assign the LGR6 polypeptide of SEQ ID NO: 5 to the GPCR subfamily I or the subgroup of GPCR subfamily I, such an assignment still does not render a specific biological function and thus a well-established utility for the LGR6 polypeptide of SEQ ID NO: 5 of the present invention because there is no single common biological function for the members of the GPCR subfamily I, even the subgroup of GPCR subfamily I. As acknowledged in the instant disclosure (pages 1, 2, 17, and 18 of the specification), the subfamily I comprises over 200 unique members. Even for the subgroup of GPCR subfamily, the ligands for these receptors comprise different glycoprotein hormones, such as LH, FSH, CG, and TSH (the 2nd paragraph of page 18 of the specification). While binding of a glycoprotein hormone to these receptors leads to activation of the Gs-cAMP-protein kinase A

pathway, each receptor plays a unique biological role, which is not shared among all the members of the subgroup of GPCR subfamily.

At the 3rd paragraph of page 24 of Applicants' response filed on 12/16/2005, Applicants argue that Exhibits submitted by Applicants evidence the importance of beta-adrenergic receptors and signaling pathways in the development of cardiovascular diseases, such as cardiomyopathy. Applicants argue that as LGR6 is expressed in the heart, is related to the receptors known for roles in heart failure and signals through pathways implicated in heart failure, LGR has utility in cardiovascular disorders.

Applicants' argument has been fully considered, but is not deemed to be persuasive because the instant disclosure fails to provide sufficient evidence showing that the LGR6 polypeptide of SEQ ID NO: 5 of the present invention acts in the same manner as the beta2adrenergic receptor. Sharing some sequence homology with the beta2adrenergic receptor is not sufficient to render the polypeptide of LGR6 a beta2adrenergic receptor. Both a rabbit and a cow eat grass, but a rabbit is certainly not a cow! The asserted sequence homology of the LGR6 polypeptide with the beta2adrenergic receptor and the expression of LGR6 polypeptide in brain do not represent sufficient evidence that establishes a specific biological function and thus a specific and substantial utility for the claimed nucleic acid molecules.

Beginning at the 4th paragraph of page 24 of Applicants' response filed on 12/16/2005, Applicants argue that Exhibits F and G evidence of the expectation that LGR6 plays an important functional role in the tissue where it is expressed. Applicants argue that LGR4 and LGR5 are the closest relatives to LGR6. Studies wherein the LGR4 or LGR5 gene is deleted show that homozygous mice containing such a deletion have very low, or no survival, respectively. The phenotypic hallmark of such mice is a defect in the tissue in which the LGR is normally expressed. Applicants argue that with the highest LGR6 expression in the heart, the heart is most affected by the activity or expression of LGR 6. Thus, LGR6 is an important target for diagnosis or treatment of cardiovascular disorders.

Applicants' argument has been fully considered, but is not deemed to be persuasive because both exhibits F and G, which are published after the filing date of the instant application, teach that LGR4-6 are orphan receptors with unknown physiological roles before June 13, 2005 (see abstracts of the two papers shown in Exhibits F and G). Even after the publication of the two cited papers shown in Exhibits F and G, the physiological roles of LGR4-6 still remain elusive (see, e.g., comments at the end of the two papers).

Accordingly, the asserted utility of using the expression or activity of LGR6 in the diagnosis or treatment of cardiovascular disorder is not a specific and substantial utility for the claimed nucleic acid molecules.

Claim Rejections under 35 USC § 112, Enablement

The rejection of claims 23-39 under 35 U.S.C. §112, 1st paragraph is maintained because the claimed invention is not supported by either a specific, substantial, and credible utility, or a well-established utility, one skilled in the art clearly would not know how to use the claimed invention. New claims 41 and 44 are also rejected on the same basis.

Applicants' arguments about the patentable utility of the claimed invention have been fully considered, but are not deemed to be persuasive for the reasons set forth above.

Moreover, even if the nucleic acid encoding the polypeptide of SEQ ID NO: 5 were to have a patentable utility, the instant disclosure would not be found to be enabling for the full scope of the invention of claims 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, and 39.

Claims 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, and 39 are drawn to an isolated nucleic acid molecule comprising a nucleotide sequence encoding a biological portion of an LGR6 polypeptide, an expression vector, a host cell comprising the nucleic acid molecule, and a method of producing the a biological portion of an LGR6 polypeptide. The claims do not require that the compound possesses any particular conserved structure nor other disclosed distinguishing feature. While reciting "a biological portion", the claims do not require that the claimed nucleic acid or the polypeptide encoded by the nucleic acid possess any particular biological function. The instant disclosure fails to

provide sufficient guidance and/or working examples concerning how to make and use a biologically active portion of an LGR6 polypeptide. The prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to make and use the nucleic acids that encode a biologically active portion of an LGR6 polypeptide. Accordingly, it would require undue experimentation for one skilled in the art to make and use the claimed invention commensurate in scope with the claims.

Claim Rejections under 35 USC § 112, 1st paragraph, Written Description

Claims 24, 25, 27, 28, 30, 31, 33, 34, 36, 37,and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, and 39 are drawn to an isolated nucleic acid molecule comprising a nucleotide sequence encoding a biological portion of an LGR6 polypeptide, an expression vector, a host cell comprising the nucleic acid molecule, and a method of producing the a biological portion of an LGR6 polypeptide. The claims do not require that the compound possesses any particular conserved structure nor other disclosed distinguishing feature. While reciting "a biological portion", the claims do not require that the claimed nucleic acid or the polypeptide encoded by the nucleic acid possess any particular biological function.

The instant disclosure of two isolated nucleic acids set forth in SEQ ID NO: 4 and SEQ ID NO: 6 that encode a polypeptide of SEQ ID NO: 5 does not adequately support the scope of the claimed genus of compounds. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). While disclosing the nucleic acid encoding the polypeptide of SEQ ID NO: 5, the instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the claimed genus of compounds. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of

structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed nucleic acid molecules as being identical to those instantly claimed. Thus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the claimed genus.

Claim Objections

Claims 23 and 41 are objected to because of the following informalities: (i). There is a typographic error in line 3 of claim 23: "a)" should be deleted; (ii). Claim 41 recites "an amino acid sequence of SEQ ID NO: 5 in line 2. The article, "the", should be used instead of "a". Appropriate correction is required.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [Brenda.Brumback@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Ruixiang Li

RUIXIANG LI, PH.D.
PRIMARY EXAMINER

Ruixiang Li, Ph.D.
Primary Examiner
March 3, 2006